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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,776	06/21/2002	Kei Tashiro	29288.5600	2614

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EXAMINER	
HAQ, SHAFIQUL	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 07/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/089,776	TASHIRO ET AL.	
	Examiner	Art Unit	
	Shafiqul Haq	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 May 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9-12 and 14-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9-12 and 14-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' arguments and amendment filed 5/12/06 have been acknowledged and entered.

2. Claims 8 and 13 have been cancelled and therefore, claims 1-7, 9-12 and 14-16 are pending and under active prosecution.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-7 and 9-12 and 14-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claim 1 recites the term "non-denaturing temperature conditions for cytokine". It is unclear what temperature (s) is/are considered as "non-denaturing temperature for cytokines" because "non-denaturing temperature for cytokines" is not defined in the specification.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over each of 1) Yuan et al (Anal. Chem. 1998, Vol. 70, No.3, pp. 596-601) or Matsumoto et al (US

5,859,297) and in view of 2) Pennanen et al (Int. J. Immunopharmacol. 1995, Vol. 17, No. 6, pp. 475-480).and further in view of Wagner et al. (US4,680,275).

The claims of the present application recite a time-resolved fluorescent immunoassay method for detection of cytokine in biological sample using a streptavidin (or avidin)-lanthanide metal ions conjugate.

Yuan et al disclose a time resolved immunoassay method for detection of alpha-fetoprotein in biological sample (serum) (see title and abstract) comprising the following: (a) anti AFP antibody (first antibody) including a portion bound to a solid-phase and a region bindable to AFP; (b) the AFP; (c) a second antibody including a region bindable to the AFP and a portion to which biotin is bound; and (d) a conjugate including streptovidin (SA) and a fluorescent structure portion (BHHCT) capable to being complexed with a lanthanide metal ion (Eu+3) (see page 597, fig 1 and page 598, fig.2). The fluorescent structure portion of fig.1 (BHHT and BHHCT) anticipate formula (I) and (III) of the present application. Fluorescence is measured after composite is formed on the solid phase and both solid phase measurement and after dissolution measurement are disclosed (page 598, fig.2).

Matsumoto et al. also disclosed time resolved immunoassay method for detection (both solid phase and liquid phase measurement) of alpha-fetoprotein in a sample (see abstract and column 24, lines 15-20). The fluorescent structural portion of formulas (I), (II) and (III) of claims 1, 3 and 4 of the present inventions are disclosed in this reference (see abstract; column 2, formula (1), (2) and (3); column 19, compound (j') and (j)) that are labeled with avidin or streptavidin (column 15,

lines 55-62; column 20, lines 63-67) and complexed with lanthanide metal ions (column 5, lines 35-37 and column 25, lines 15-20). The time-resolved fluoroimmunoassy for detection of AFP includes first antibody (anti-human AFP)(column 23, line 29), human AFP (column 23, line 45), a biotinylated second antibody (biotinylated goat anti-rabbit antibody) (column 23, lines 57-58) and a streptavidin-(fluorescent structural portion)-Eu^{+3} complex (SA-BHHCT-Eu^{+3}) (column 23, lines 65-66).

Both Yaun et al and Matsumoto et al. disclose that use of β-diketone ligand (BHHCT) improves detection sensitivity. Yaun et al. discloses that use of β-diketone ligand (BHHCT) gave remarkable superiority over conventional organic fluorescent labels and other lanthanide labels in time resolved fluorometric determination of AFP as the detection limits are greatly improved (page 597) and Matsumoto et al. also disclose that the use of SA-BHHCT-Eu^{3+} in a time-resolved immunoassay, remarkably improved the detection limit of AFP (from 1ng/ml to 10^{-6}ng/ml; column 24, lines 15-25). Therefore, incorporation of β-diketone fluorescent structure portion (BHHCT) is desirable for detection of low level analytes by time-resolved immunoassay.

Although Yuan et al and Matsumoto et al. disclose detection of alpha-fetoprotein in biological sample employing streptavidin-(fluorescent structural portion)-lanthanide complex (e.g. SA-BHHCT-Eu^{+3}) in time-resolved fluoroimmunoassay, but they fail to disclose detection of cytokine in biological fluids as claimed in the present applicaiton.

Pennanen et al disclose detection of cytokine in a sample by time-resolved fluoroimmunoassay comprising primary antibody (first antibody) bound to solid phase (e.g. microtiter strips), biotinylated second antibody and europium labeled streptavidin (see title and page 476, right column, lines 13-48). Pennanen et al. refer to cytokines and other cytokines (page 479, line 5 of 1st paragraph, right column) and do not exclude chemokines (i.e chemotactic cytokines).

Since, detection of cytokine by time-resolved fluoroimmunoassy using lanthanide-streptavidin complex is common and know in the art (Pennanen et al) and use of β-diketone ligand (BHHCT) is desirable in time-resolved fluoroimmunoassay as it greatly improves detection sensitivity (Yuan et al or Matsumoto et al), it would have been obvious at the time of the invention to a person of ordinary skill in the art to include cytokine as an equivalent analyte for detection in the method of Yuan et al or Matsumoto et al, with the expectation of detecting/measuring of cytokine with a high sensitivity in a sample with a reasonable expectation of success. Since it is known that cytokines are present in biological samples in low concentration, one would be motivated to use the techniques of the primary references to enhance the fluorescence detection of the low level analyte.

The above paragraphs, disclose a time-resolved fluorescent immunoassay method for detection of cytokine in biological sample using a streptavidin (or avidin)-lanthanide metal ions conjugate comprising β-diketone ligand (BHHCT) but, fail to disclose the components in a kit format.

Wagner et al. disclose time-resolved Fluorescence immunoassay method utilizing lanthanide ion such as europium or terbium chelated with organic ligand such as beta-diketone for sensitive detection of analyte in a sample. The invention also provides a reagent kit or package of materials for accomplishing an assay for an analyte in accordance with the method of the invention.

Since, packaging of immunoassay components as a kit format is common and well known in the art (Wagner et al), it would have been obvious at the time of the invention to a person of ordinary skill in the art to provide Yuan et al or Matsumoto et al with components of the immunoassy as a kit format for ease and convenience in assay performance.

Response to Argument

8. Applicant's arguments and amendments filed 5/12/06 have been fully considered and are persuasive to overcome the rejections under 35 USC 103 for claims 1-7, 9-12 and 14-15 but are not persuasive to overcome the rejection of claim 16 (kit composition) under 35 USC 103. Applicants' amendment also raised new issues under 35 USC 112, second paragraph that is discussed in paragraph 5 of this office action.

With respect to kit composition of claim 16, obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fines, 837 F.2d 1071, 5USPQ2d 1596 (Fed. Cir.

1988) and In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir.1992). In this case, both Yaun and Matsumoto disclose solid phase time resolved immunoassay method using β-diketone ligand (BHHCT) and Wagner et al. disclose that immunoassay components for solid phase immunoassay can be provided as a reagent kit or package of materials for accomplishing an assay for an analyte (see column 7, lines 29-45) and Wrangler et al. also disclose use of β-diketone ligand (see column 5, lines 1-14). Also, the packaging of components in kit form is a well-known obvious expedient for ease and convenience in assay performance and once a method has been established, one skilled in the art would clearly consider compiling in a kit format and change/modify different components of the kit to best suit the assay.

With respect to incorporation of term "non-denaturing temperature conditions for cytokine" in claim 1, "non-denaturing temperature" is not defined in the specification and it is not clear what temperature Applicant is intended to claim. In remarks of 5/12/06, Applicants states "heating plasma samples under non-denaturing temperature conditions leads to increased sensitivity of detection (as evidenced in figure 3b)". Applicants' attention is drawn to page 63, lines 12-16 of the specification, which recites "heating at 37°C or 55°C for 30 minutes yielded substantially the same calibration curve as those of the non-heated samples, and did not affect the detected amount of SDF-1". This statement is contrary to Applicants' remarks of 5/12/06 and Applicant is advised to clarify this statement. However,

specification has guidance and examples of heat treatment of sample at 55°C for 30 minutes that results in the enhancement in fluorescence intensity (see fig. 3b and pages 13, 63 and 64) but there is no guidance and example for other conditions (i.e. heating at other temperature) that resulted in improved sensitivity.

Conclusion

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shafiqul Haq whose telephone number is 571-272-6103. The examiner can normally be reached on 7:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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